Request — Jan Delaval

Access DB# 16138

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabiha Qazi Examiner #: 74141 Date: 8/2/05
Art Unit: 1616 Phone Number 30 206 22 Serial Number: 10/780,103
Mail Box and Bldg/Room Location: 4C70 Rem, 4A45 Results Format Preferred (circle): PAPER, DISK E-MAIL
If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: 26,27-Homologated-20-epi-2-alkylidene-19-
Inventors (please provide full names): De Luca et al V.t.D comp

Earliest Priority Filing Date: 3/17/1997

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for method of treating selective Cancerous disease. as in cls 49, 54-58; 59-68; 69-78 and 78 to 88.

Please see attached sheet

Thank you

STAFF USE ONLY

Searcher: Ann
Searcher Phone #: 02504
Searcher Location:
Date Searcher Picked Up: 8/5/05
Date Completed: 8/5/05
Searcher Prep / Review Time:
Clerical Prep Time: 15
Online Time: 110

Type of Search
NA Sequence (#)
AA Sequence (#)
Structure (#) 4
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable
STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet 0
Other (specify)

PTO-1590 (8-01)

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FILE 'REGISTRY' ENTERED AT 15:22:48 ON 05 AUG 2005
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:    4 AUG 2005  HIGHEST RN 858414-27-4
DICTIONARY FILE UPDATES:   4 AUG 2005  HIGHEST RN 858414-27-4

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d l12 ide can tot

L12  ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   364059-51-8  REGISTRY
ED   Entered STN:  23 Oct 2001
CN   19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-
     methylene-, (1α,3β,7E,20S)- (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C29 H46 O3
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.
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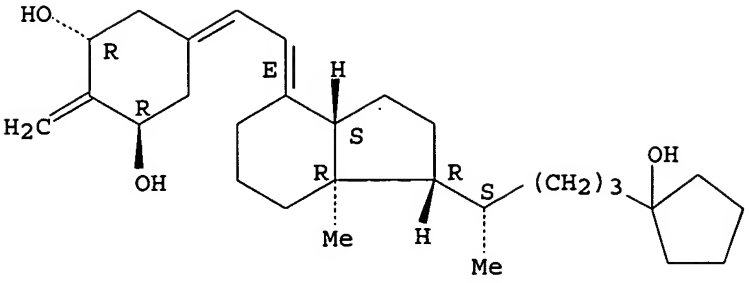

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:401925

REFERENCE 2: 136:380526

REFERENCE 3: 135:358086

REFERENCE 4: 135:304063

REFERENCE 5: 135:288953

L12 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN
RN **364059-50-7** REGISTRY
ED Entered STN: 23 Oct 2001
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)
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LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

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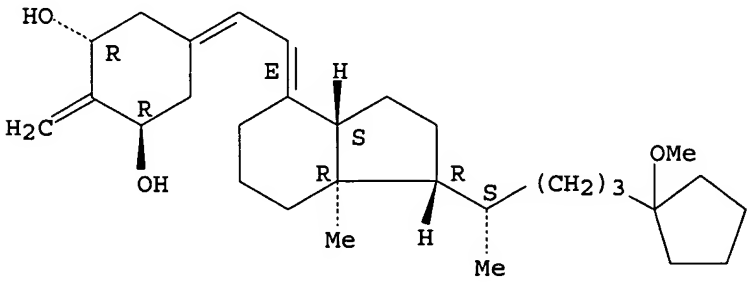

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LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

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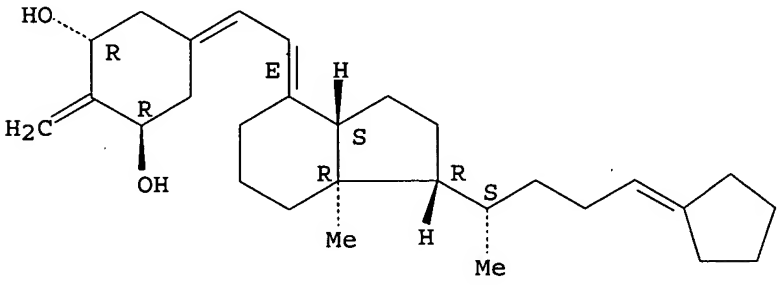
Double bond geometry as shown.



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REFERENCE 2: 135:358086

REFERENCE 3: 135:304063

REFERENCE 4: 135:288953

L12 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN
RN **364059-44-9** REGISTRY
ED Entered STN: 23 Oct 2001
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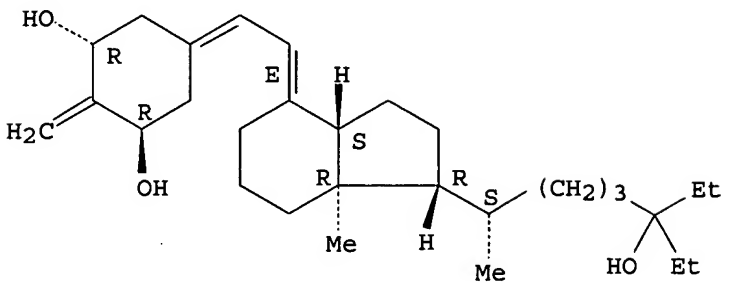
FS STEREOSEARCH
MF **C29 H48 O3**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



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SEL RN

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L3 8 S L2 AND C5-C6/ES AND 46.150.1/RID AND 3/NR
L4 5 S L2 AND C5-C6/ES AND 46.150.1/RID AND C5/ES AND 4/NR
L5 1 S L3 AND C29H48O3
L6 51 S C29H48O3 AND C5-C6/ES AND 46.150.1/RID
L7 49 S L6 AND 3/NR
L8 3 S L4 NOT SI/ELS
L9 1884 S C30H48O3 OR C29H46O3 OR C29H44O2
L10 4 S L9 AND C5-C6/ES AND 46.150.1/RID AND C5/ES AND 4/NR
L11 3 S L10 NOT 114694-10-9
L12 4 S L5,L8,L11
SAV L12 QAZI780/A

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L13 0 S L12

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L16             5 S L14 AND (DELUCA ? OR DE LUCA ? OR LUCA ? OR SICINSKI ?)/AU

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=> fil uspatful
FILE 'USPATFULL' ENTERED AT 15:22:59 ON 05 AUG 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 4 Aug 2005 (20050804/PD)
FILE LAST UPDATED: 4 Aug 2005 (20050804/ED)
HIGHEST GRANTED PATENT NUMBER: US6925651
HIGHEST APPLICATION PUBLICATION NUMBER: US2005172377
CA INDEXING IS CURRENT THROUGH 4 Aug 2005 (20050804/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 4 Aug 2005 (20050804/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

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>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L17  ANSWER 1 OF 2  USPATFULL on STN
AN     2002:116429  USPATFULL
TI     26,27-homologated-20-EPI-2-alkylidene-19-nor-vitamin D compounds
IN     DeLuca, Hector F., Deerfield, WI, United States
       Sicinski, Rafal R., Warsaw, POLAND
PA     Wisconsin Alumni: Research Foundation, Madison, WI, United States (U.S.
       corporation)
PI     US 6392071         B1   20020521
AI     US 2000-540686          20000331 (9)
RLI    Continuation-in-part of Ser. No. US 1999-370966, filed on 10 Aug 1999,
       now abandoned Continuation of Ser. No. US 1998-151113, filed on 10 Sep
       1998, now patented, Pat. No. US 5936133 Division of Ser. No. US
       1997-819693, filed on 17 Mar 1997, now patented, Pat. No. US 5843928
DT     Utility
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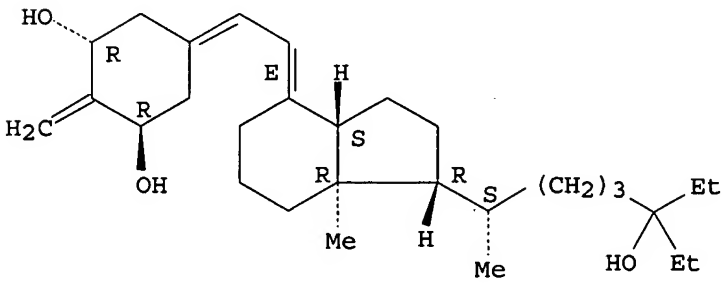
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1372
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, the 2-alkylidene-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 and R.sub.8, which may be the same or different, are each selected from hydrogen, alkyl, hydroxyalkyl and fluoroalkyl, or when taken together represent the group --(CH.sub.2).sub.x-- where x is an integer from 2 to 5, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

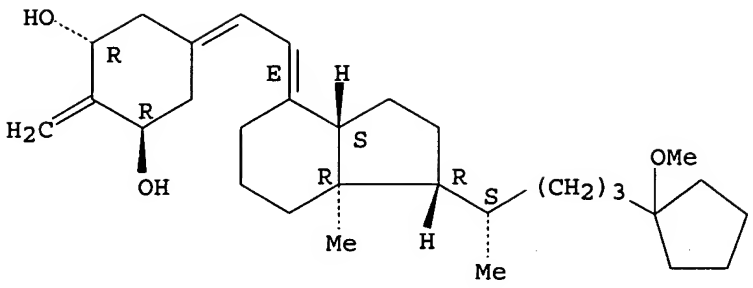
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **364059-44-9P 364059-50-7P 364059-51-8P**
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RN 364059-44-9 USPATFULL
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



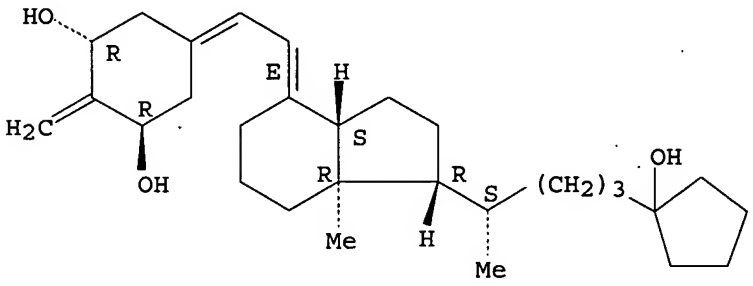
RN 364059-50-7 USPATFULL
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 USPATFULL
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L17 ANSWER 2 OF 2 USPATFULL on STN
AN 2001:202815 USPATFULL
TI 26,27-Homologated-20-EPI-2alkyl-19-nor-vitamin D compounds
IN DeLuca, Hector F., Deerfield, WI, United States
Sicinski, Rafal R., Warsaw, Poland
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6316642 B1 20011113
AI US 2000-541470 20000331 (9)
RLI Continuation-in-part of Ser. No. US 1999-454013, filed on 3 Dec 1999 Division of Ser. No. US 1998-135463, filed on 17 Aug 1998, now patented, Pat. No. US 6127559 Continuation-in-part of Ser. No. US 1997-819694, filed on 17 Mar 1997, now patented, Pat. No. US 5945410
DT Utility
FS GRANTED
EXNAM Primary Examiner: Qazi, Sabiha
LREP Andrus, Sceales, Starke & Sawall, LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1931
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a novel class of vitamin D related compounds, namely, 2-alkyl-19-nor-vitamin D derivatives, as well as a general method for their chemical synthesis. The compounds have the formula: ##STR1##

where Y.sub.1 and Y.sub.2, which may be the same or different, are each

selected from the group consisting of hydrogen and a hydroxy-protecting group, R.sub.6 is selected from the group consisting of alkyl, hydroxyalkyl and fluoroalkyl, and where the group R represents any of the typical side chains known for vitamin D type compounds. These 2-substituted compounds, especially the 2α-methyl and the 2α-methyl-20S derivatives, are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compounds also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

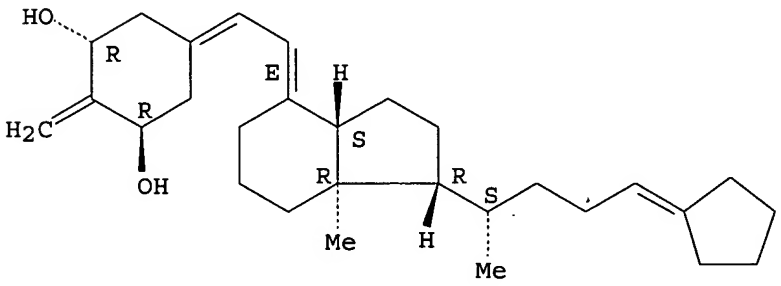
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **364059-49-4P 364059-50-7P**
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 364059-49-4 USPATFULL

CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-cyclopentylidene-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

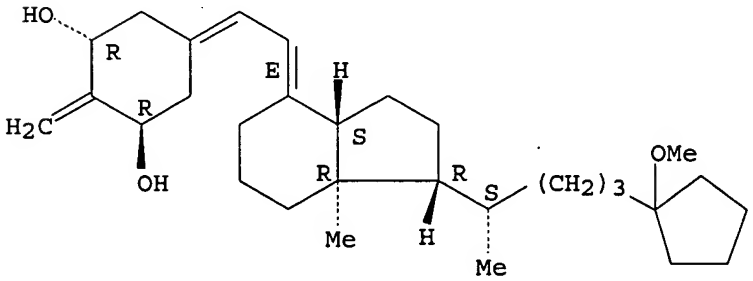
Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-50-7 USPATFULL

CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

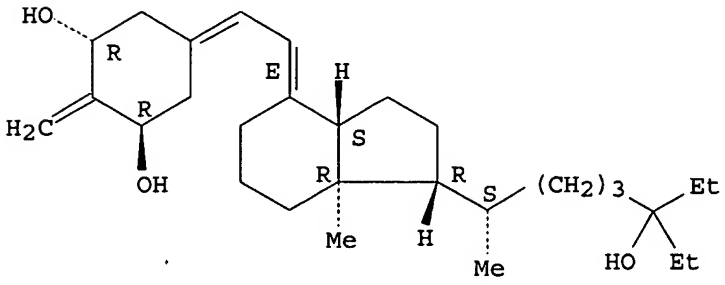


IT **364059-44-9P 364059-51-8P**
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 364059-44-9 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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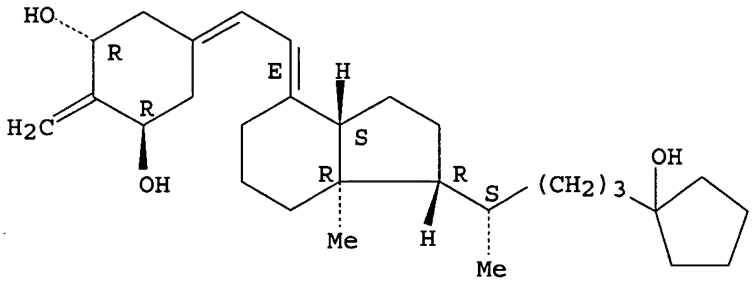
Absolute stereochemistry.
Double bond geometry as shown.



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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 5 Aug 2005 VOL 143 ISS 7
FILE LAST UPDATED: 4 Aug 2005 (20050804/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L16 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:387626 HCAPLUS
DN 136:401925
ED Entered STN: 23 May 2002
TI Preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
IN **Deluca, Hector F.; Sicinski, Rafal R.**
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 370,966, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07C401-00
ICS A61K031-593
INCL 552653000
CC 32-7 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 3

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PI	US 6392071	B1	20020521	US 2000-540686	20000331
	US 5843928	A	19981201	US 1997-819693	19970317
	US 5936133	A	19990810	US 1998-151113	19980910
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	WO 2001074766	A1	20011011	WO 2001-US10317	20010329
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	NZ 522160	A	20041126	NZ 2001-522160	20010329
	US 2002087015	A1	20020704	US 2001-1711	20011031
	US 6537981	B2	20030325		
	US 2003181427	A1	20030925	US 2003-352745	20030128
	US 6696431	B2	20040224		
	US 2004167104	A1	20040826	US 2004-780103	20040217
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

US 6392071	ICM	C07C401-00
	ICS	A61K031-593
	INCL	552653000
US 6392071	NCL	552/653.000
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US 5843928	NCL	514/167.000; 552/653.000
	ECLA	C07C401/00; C07F007/18C4D4D; C07F007/18C4D4C
US 5936133	NCL	568/828.000; 556/436.000; 556/437.000; 556/482.000; 560/126.000; 560/128.000; 568/014.000; 568/470.000
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WO 2001074766	ECLA	C07C401/00
US 2002087015	NCL	514/167.000; 552/653.000
	ECLA	C07C401/00; C07F007/18C4D4C; C07F007/18C4D4D
US 2003181427	NCL	514/167.000; 552/653.000
	ECLA	C07C401/00; C07F007/18C4D4C; C07F007/18C4D4D
US 2004167104	NCL	514/167.000
	ECLA	C07C401/00; C07F007/18C4D4C; C07F007/18C4D4D

OS MARPAT 136:401925
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R6, R8 = alkyl, hydroxyalkyl, fluoroalkyl, etc., or when taken together represent the group -(CH2)x- where x is an integer from 2 to 5; R = any of the typical side chains known for vitamin D type compds.] are prepared These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. Thus, 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-nor-vitamin D3 (II) was prepared via a multistep synthetic sequence starting from 20(S)-25-hydroxy Grundmann's ketone analog III and phosphine oxide IV. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in vitamin D-deficient rats on a low calcium diet responding to chronic doses of II at 15 pmol/day/7 days were 4.0 ± 0.4 S/M and 5.3 ± 0.1 S/M resp. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

ST vitamin D nor alkylidene prepn antiosteoporotics calcium mobilization; antitumor alkylidene nor vitamin D prepn treatment psoriasis

IT Biological transport
(calcium; preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 9,10-Secosteroids
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
IT Osteoporosis
(therapeutic agents; preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
IT Bone, disease
Psoriasis
(treatment; preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
IT 213250-70-5P 213319-29-0P **364059-44-9P 364059-50-7P 364059-51-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
IT 1779-49-3, Methyltriphenylphosphonium bromide 2916-76-9, Methyl(trimethylsilyl)acetate 32222-06-3 135711-62-5 144848-24-8 213250-67-0 364059-41-6 364059-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
IT 213250-58-9P 213250-59-0P 213250-60-3P 213250-61-4P 213250-62-5P 213250-63-6P 213250-64-7P 213250-65-8P 213250-68-1P 213250-69-2P 364059-42-7P 364059-43-8P 364059-47-2P 364059-48-3P 428817-35-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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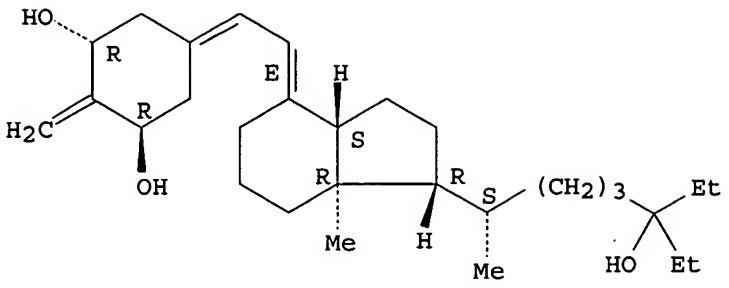
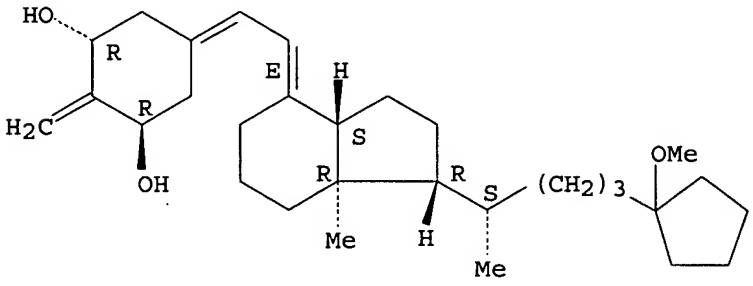
(2) Deluca; US 4800198 A 1989 HCAPLUS
(3) Deluca; US 4851401 A 1989 HCAPLUS
(4) Deluca; US 5089641 A 1992 HCAPLUS
(5) Deluca; US 5587497 A 1996 HCAPLUS
(6) Deluca; US 5945410 A 1999 HCAPLUS
(7) Deluca; US 5981780 A 1999 HCAPLUS
(8) Paaren; US 5936105 A 1999 HCAPLUS
(9) Sicinski; J Med Chem 1998, P4662 HCAPLUS
(10) Yang; Journal of Biological Chemistry 1999, P16838 HCAPLUS
IT **364059-44-9P 364059-50-7P 364059-51-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RN 364059-44-9 HCAPLUS
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



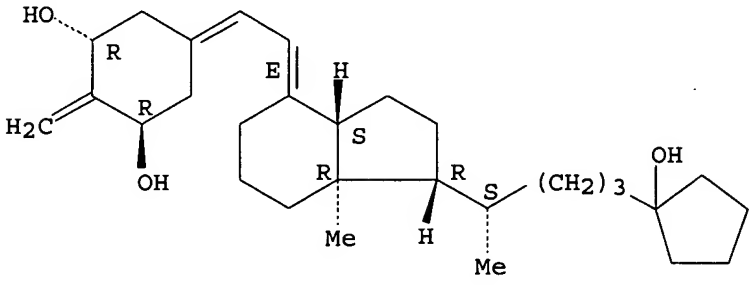
RN 364059-50-7 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 2 OF 5. HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:133888 HCAPLUS
DN 136:380526
ED Entered STN: 20 Feb 2002
TI New highly calcemic 1α,25-dihydroxy-19-norvitamin D3 compounds with modified side chain: 26,27-dihomo- and 26,27-dimethylene analogs in 20S-series
AU **Sicinski, Rafal R.**; Prahl, Jean M.; Smith, Connie M.;

DeLuca, Hector F.
CS Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA
SO Steroids (2002), 67(3,4), 247-256
CODEN: STEDAM; ISSN: 0039-128X
PB Elsevier Science Inc.
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB New highly potent 2-substituted (20S)-1α,25-dihydroxy-19-norvitamin D3 analogs with elongated side chain were prepared by Wittig-Horner coupling of A-ring phosphine oxide with the corresponding protected (20S)-25-hydroxy Grundmann's ketones. Biol. evaluation in vitro and in vivo of the synthesized compds. was accomplished. All the synthesized vitamins possessing a 25-hydroxylated saturated side chain were slightly less active (3-5X) than 1α,25-dihydroxyvitamin D3 in binding to the porcine intestinal vitamin D receptor and significantly more potent (12-150X) in causing differentiation of HL-60 cells. In vivo, 2-methylene-26,27-dihomo and 2α-methyl-26,27-dimethylene analogs were at least 10 times more active, and 2α-methyl-26,27-dihomo compound at least 5 times more active than the vitamin D hormone both in stimulating intestinal calcium transport and bone calcium mobilization (serum calcium increase). It was also established that a 260 pmol dose of the corresponding 2β-Me analogs had a similar effect on intestinal calcium transport and a much more pronounced effect on bone calcium mobilization as the same dose of 1α,25-dihydroxyvitamin D3.
ST dihydroxyvitamin D3 analog biol activity structure; vitamin D receptor binding calcitriol analog structure; calcium transport bone intestinal calcitriol analog structure; cell differentiation calcitriol analog structure

IT Bone
Cell differentiation
Intestine
Molecular modeling
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT Vitamin D receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT Structure-activity relationship
(calcium-mobilizing; calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT Biological transport
(calcium; calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT Structure-activity relationship
(cell differentiation-affecting; calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT Structure-activity relationship
(receptor-binding; calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT 32222-06-3, Calcitriol
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

IT **364059-44-9P 364059-51-8P**
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)
IT 195051-26-4DP, dihomo and dimethylene analogs 364059-45-0P
364059-49-4P 364059-50-7P 364059-52-9P 372965-48-5P
372965-49-6P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)
IT 364059-42-7P 364059-43-8P 364059-47-2P 364059-48-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)
IT 213250-64-7 364059-41-6 364059-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Binderup, L; Biochem Pharmacol 1991, V42, P1569 HCAPLUS
(2) Binderup, L; Biochem Pharmacol 1992, V43, P1885 HCAPLUS
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(27) Sicinski, R; J Med Chem 1998, V41, P4662 HCAPLUS
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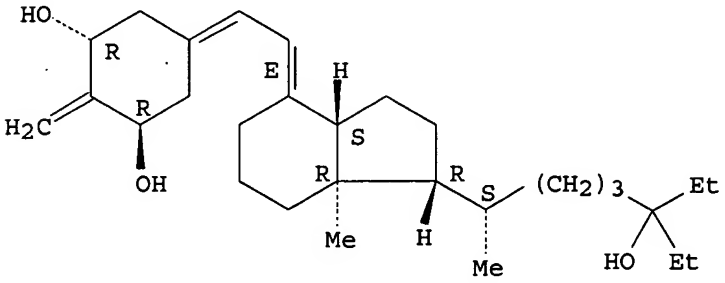
(35) Yu, X; Proc Natl Acad Sci USA 1991, V88, P8347 HCAPLUS

IT **364059-44-9P 364059-51-8P**
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

RN 364059-44-9 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

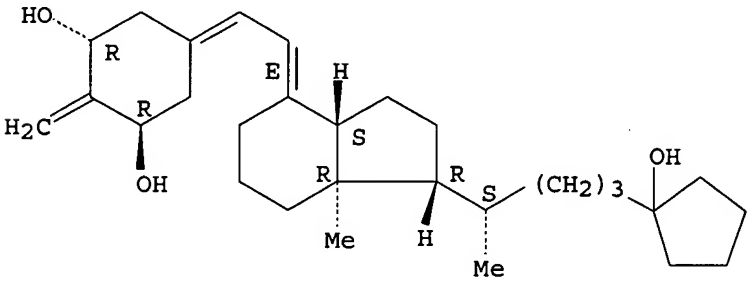
Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 HCAPLUS

CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

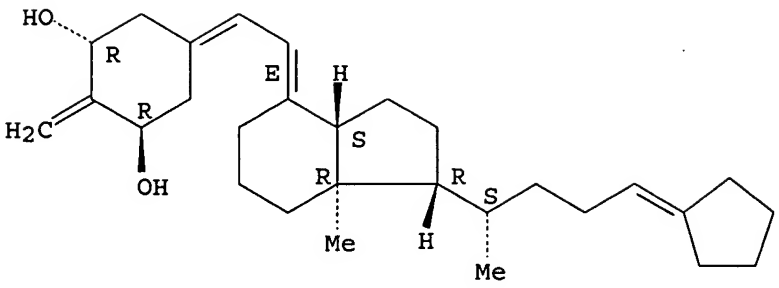


IT **364059-49-4P 364059-50-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(calcitriol analogs preparation and vitamin D-binding, calciotropic and cell differentiating activity)

RN 364059-49-4 HCAPLUS

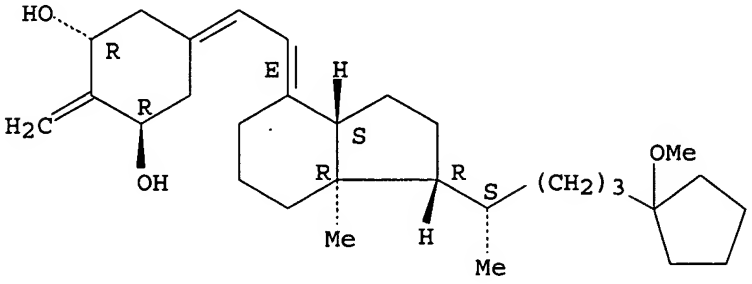
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-cyclopentylidene-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-50-7 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:830900 HCAPLUS
DN 135:358086
ED Entered STN: 15 Nov 2001
TI Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN **Deluca, Hector F.; Sicinski, Rafal R.**
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 454,013.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07C401-00
ICS A61K031-59
INCL 552653000
CC 32-7 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 6

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	US 5945410	A	19990831	US 1997-819694	19970317
	US 6127559	A	20001003	US 1998-135463	19980817
	US 6277837	B1	20010821	US 1999-454013	19991203
	CA 2403232	AA	20011011	CA 2001-2403232	20010329
	WO 2001074765	A1	20011011	WO 2001-US10094	20010329

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    US 2002123638       A1    20020905    US 2001-999299          20011031
    US 6544969          B2    20030408
    US 2003073857       A1    20030417    US 2002-246968          20020919
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    US 2004072804       A1    20040415    US 2003-673618          20030929
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PRAI US 1997-819694     A2    19970317
    US 1998-135463      A3    19980817
    US 1999-454013      A2    19991203
    US 2000-541470      A     20000331
    WO 2001-US10094     W     20010329
    US 2001-45941       B3    20011019
    US 2001-999299      A3    20011031
    US 2002-246968      A3    20020919
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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                  ICS    A61K031-59
                  INCL   552653000
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                  ECLA   C07C401/00
 US 5945410       NCL    514/167.000; 552/653.000
                  ECLA   C07C401/00
 US 6127559       NCL    552/653.000
                  ECLA   C07C401/00
 US 6277837       NCL    514/167.000; 552/653.000
                  ECLA   C07C401/00
 WO 2001074765    ECLA   C07C401/00
 JP 2004500414    FTERM  4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/DA16;
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                         4H006/UA52
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                  ECLA   C07C401/00
 US 2004072804    NCL    514/167.000
                  ECLA   A61K031/56; A61K031/59
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                  ECLA   C07C401/00
OS   MARPAT 135:358086
GI
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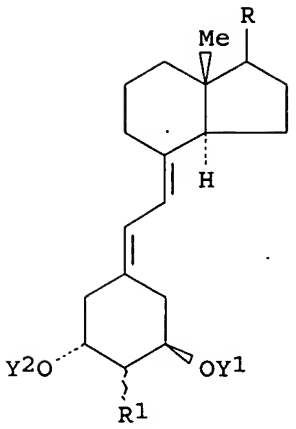

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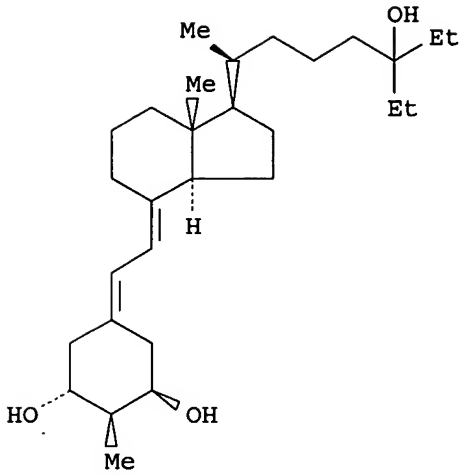


II

AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R = typical side chains known for vitamin D type compds.; R1 = alkyl, hydroxyalkyl, fluoroalkyl] are prepared These 2-substituted compds., especially the 2α-Me and the 2α-methyl-20S derivs., are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II was prepared and showed preferential activity on bone in biol. activity tests.

ST vitamin D epi nor homologated prepn calcium transport; osteoporosis vitamin D epi nor homologated; psoriasis vitamin D epi nor homologated; asthma vitamin D epi nor homologated

IT Biological transport
(calcium; preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT Antitumor agents
Asthma
Osteoporosis
Psoriasis
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT 9,10-Secosteroids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT Vitamin D receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT 213319-30-3P 213332-83-3P 217446-51-0P 217446-52-1P 217446-53-2P

217446-54-3P 217446-55-4P 217446-56-5P 364059-45-0P
364059-49-4P 364059-50-7P 364059-52-9P 372965-48-5P
372965-49-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT 77-95-2, (-)-Quinic acid 144848-24-8 213250-67-0 364059-41-6
364059-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

IT 135711-62-5P 213250-58-9P 213250-59-0P 213250-60-3P 213250-61-4P
213250-62-5P 213250-63-6P 213250-64-7P 213250-65-8P 213250-68-1P
213250-69-2P 213250-70-5P 213319-29-0P 364059-42-7P 364059-43-8P
364059-44-9P 364059-47-2P 364059-48-3P **364059-51-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; EP 0184206 1985 HCAPLUS
(2) Anon; EP 0078704 1987 HCAPLUS
(3) Anon; 1989 HCAPLUS
(4) Anon; EP 0387077 1990 HCAPLUS
(5) Anon; WO 9009991 1990 HCAPLUS
(6) Anon; EP 0474517 1992 HCAPLUS
(7) Anon; EP 0480572 1992 HCAPLUS
(8) Anon; EP 0516410 1992 HCAPLUS
(9) Anon; WO 9601811 1996 HCAPLUS
(10) Anon; Chemical Abstracts 1994, V121(21)
(11) Baggiolini; Journal of Organic Chemistry 1986, V51, P3098 HCAPLUS
(12) Bouillon; Bioactivity of 19-Nor-Pre D 1993, V8(8), P1009 HCAPLUS
(13) Brenner; US 5849726 1998 HCAPLUS
(14) Deluca; US 5086191 1992 HCAPLUS
(15) Deluca; US 5237110 1993 HCAPLUS
(16) Deluca; US 5246925 1993 HCAPLUS
(17) Deluca; US 5536713 1996 HCAPLUS
(18) Deluca; US 5587497 1996 HCAPLUS
(19) Deluca; US 5843927 1998 HCAPLUS
(20) Kiegiel; Tetrahedron Letters 1991, V31(43), P6057
(21) Kutner; US 5817648 1998 HCAPLUS
(22) Labrie; US 5846960 1998 HCAPLUS
(23) Miyamoto; US 4666634 1987 HCAPLUS
(24) Miyamoto; US 5877168 1999 HCAPLUS
(25) Okano; Biochemical and Biophysical Research Communications 1989, V163(3), P1444 HCAPLUS
(26) Perlman; Tetrahedron Letters 1990, V31(13), P1823 HCAPLUS
(27) Posner; Journal of Organic Chemistry 1995, V56, P4339
(28) Posner; Journal of Organic Chemistry 1995, V60, P4617 HCAPLUS
(29) Sarandeses; tetrahedron Letters 1992, P5445 HCAPLUS
(30) Sicinski; Journal of Medical Chemistry 1998, V41, P4662 HCAPLUS
(31) Slatopolsky; American Journal of Kidney Disorders 1995, V26(5), P832

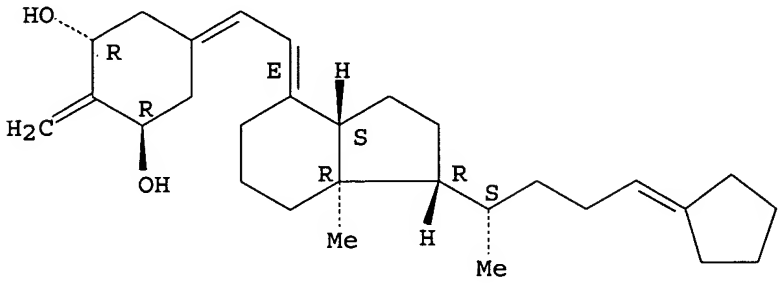
IT **364059-49-4P 364059-50-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds.

with high intestinal calcium transport activity)

RN 364059-49-4 HCAPLUS

CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-cyclopentylidene-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

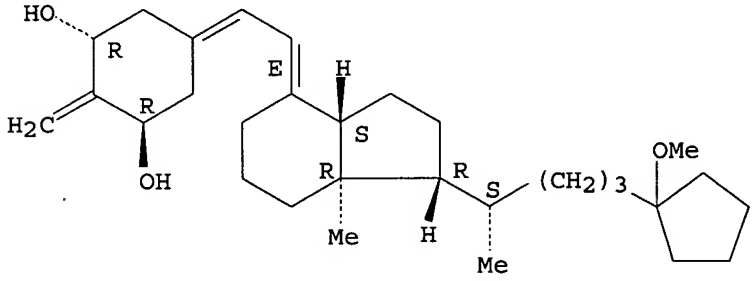
Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-50-7 HCAPLUS

CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

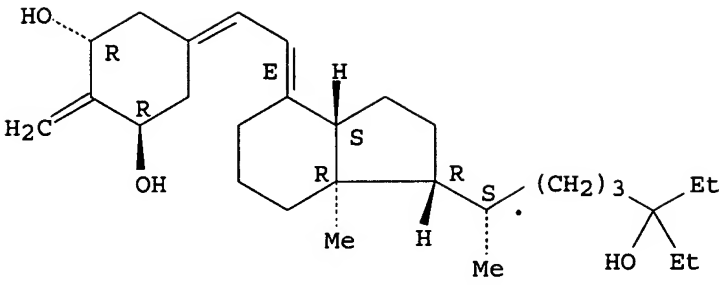


IT **364059-44-9P 364059-51-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 364059-44-9 HCAPLUS

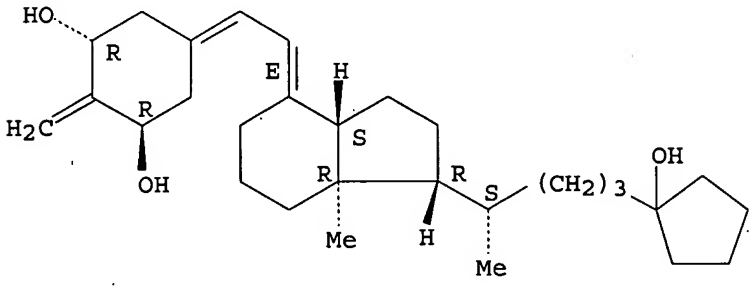
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:747743 HCAPLUS
DN 135:288953
ED Entered STN: 12 Oct 2001
TI Preparation of 2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
IN **Deluca, Hector F.; Sicinski, Rafal R.**
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C401-00
ICS A61K031-59; A61P003-02; A61P003-14; A61P017-06; A61P035-00; A61P035-02
CC 32-7 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001074766	A1	20011011	WO 2001-US10317	20010329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

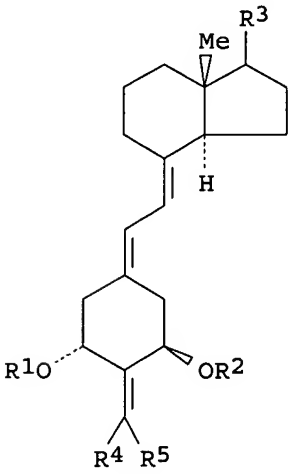
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6392071 B1 20020521 US 2000-540686 20000331
CA 2404548 AA 20011011 CA 2001-2404548 20010329
EP 1268416 A1 20030102 EP 2001-920897 20010329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003529581 T2 20031007 JP 2001-572461 20010329
NZ 522160 A 20041126 NZ 2001-522160 20010329
PRAI US 2000-540686 A 20000331
US 1997-819693 A3 19970317
US 1998-151113 A1 19980910
US 1999-370966 B2 19990810
WO 2001-US10317 W 20010329

CLASS

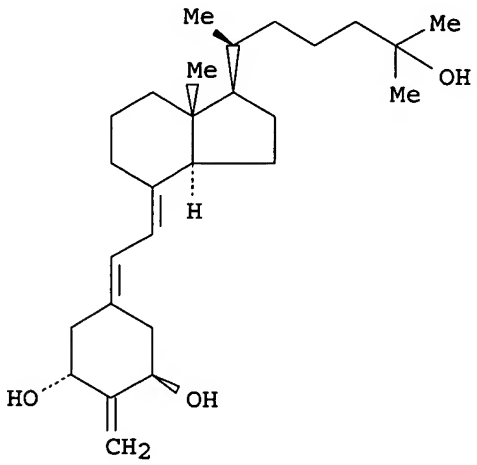
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001074766	ICM	C07C401-00
	ICS	A61K031-59; A61P003-02; A61P003-14; A61P017-06; A61P035-00; A61P035-02
WO 2001074766	ECLA	C07C401/00
US 6392071	NCL	552/653.000
	ECLA	C07C401/00; C07F007/18C4D4C; C07F007/18C4D4D

OS MARPAT 135:288953

GI



I



II

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = typical side chains known for vitamin D type compds.; R4, R5 = H, alkyl, hydroxyalkyl, fluoroalkyl, etc.; R4R5 = cycloalkylidene] are prepared These 2-substituted compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and is found to be extremely potent

in inducing differentiation of HL-60 cells.

ST vitamin D nor alkylidene prepn antiosteoporotic; antitumor vitamin D nor alkylidene prepn; psoriasis vitamin D nor alkylidene prepn

IT Biological transport
(calcium; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Intestine, neoplasm
(colon, inhibitors; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(colon; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(leukemia; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(mammary gland; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Mammary gland
Prostate gland
(neoplasm, inhibitors; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
Osteomalacia
Psoriasis
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 9,10-Secosteroids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(prostate gland; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Bone, disease
(renal osteodystrophy; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Osteoporosis
(therapeutic agents; preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

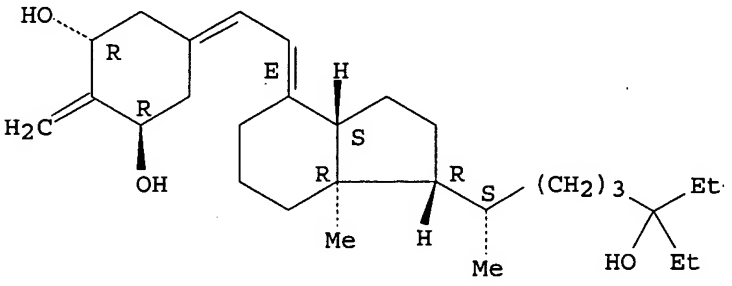
IT 213250-70-5P 213319-29-0P **364059-44-9P 364059-49-4P 364059-50-7P 364059-51-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 135711-62-5 144848-24-8 213250-67-0 364059-41-6 364059-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 213250-58-9P 213250-59-0P 213250-60-3P 213250-61-4P 213250-62-5P 213250-63-6P 213250-64-7P 213250-65-8P 213250-68-1P 213250-69-2P 364059-42-7P 364059-43-8P 364059-47-2P 364059-48-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

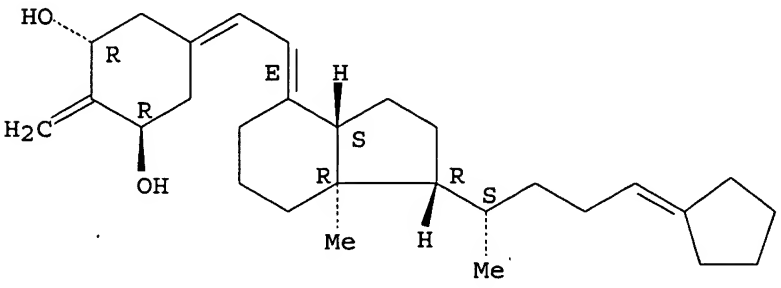
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Deluca, H; US 4851401 A 1989 HCAPLUS
(2) Deluca, H; US 5981780 A 1999 HCAPLUS
(3) Sicinski; JOURNAL OF MEDICINAL CHEMISTRY 1998, V41, P4662 HCAPLUS
(4) Wisconsin Alumni Res Found; WO 9841501 A 1998 HCAPLUS
(5) Yang; J BIOL CHEM 1999, V274(24), P16838 HCAPLUS
IT **364059-44-9P 364059-49-4P 364059-50-7P**
364059-51-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RN 364059-44-9 HCAPLUS
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



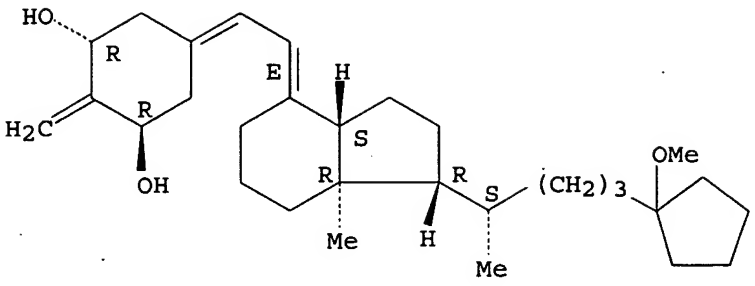
RN 364059-49-4 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-cyclopentylidene-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



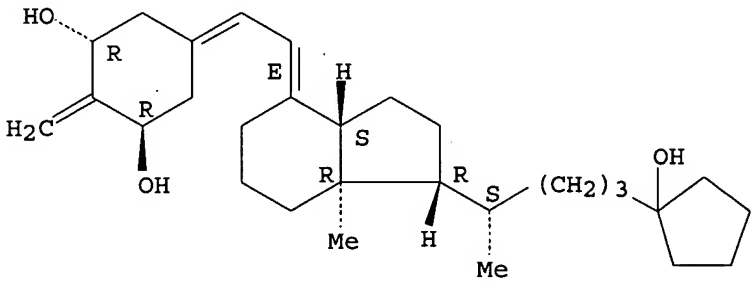
RN 364059-50-7 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L16 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:747742 HCAPLUS
DN 135:304063
ED Entered STN: 12 Oct 2001
TI Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
IN **Deluca, Hector F.; Sicinski, Rafal R.**
PA Wisconsin Alumni Research Foundation, USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C401-00
ICS A61K031-59
CC 32-7 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001074765	A1	20011011	WO 2001-US10094	20010329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 6316642	B1	20011113	US 2000-541470	20000331
	CA 2403232	AA	20011011	CA 2001-2403232	20010329
	EP 1268415	A1	20030102	EP 2001-920863	20010329
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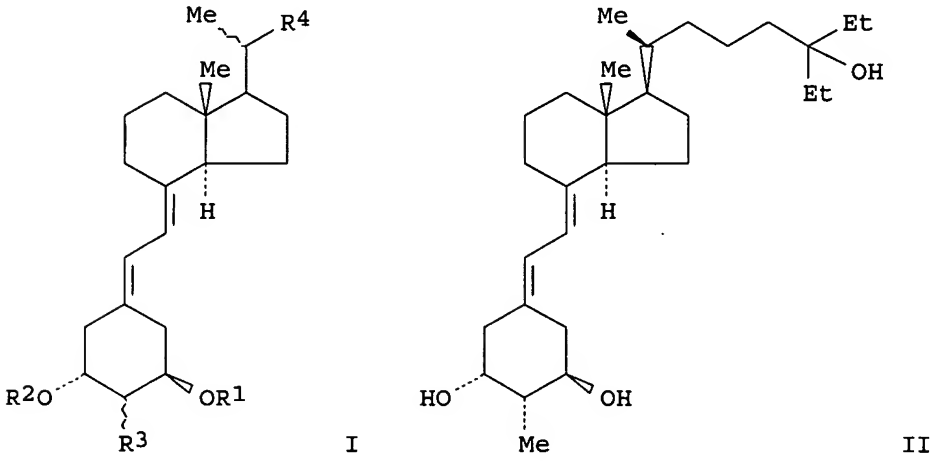
	JP 2004500414	T2	20040108	JP 2001-572460	20010329
	US 2004072804	A1	20040415	US 2003-673618	20030929
PRAI	US 2000-541470	A	20000331		
	US 1997-819694	A2	19970317		
	US 1998-135463	A3	19980817		
	US 1999-454013	A2	19991203		
	WO 2001-US10094	W	20010329		
	US 2001-45941	B3	20011019		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001074765	ICM	C07C401-00
	ICS	A61K031-59
WO 2001074765	ECLA	C07C401/00
US 6316642	NCL	552/653.000
	ECLA	C07C401/00
JP 2004500414	FTERM	4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/DA16; 4C086/MA01; 4C086/MA04; 4C086/MA13; 4C086/MA17; 4C086/MA22; 4C086/MA23; 4C086/MA28; 4C086/MA32; 4C086/MA35; 4C086/MA37; 4C086/MA41; 4C086/MA52; 4C086/MA57; 4C086/MA59; 4C086/MA63; 4C086/MA66; 4C086/NA14; 4C086/ZA89; 4C086/ZA96; 4C086/ZA97; 4C086/ZB26; 4C086/ZB27; 4C086/ZC23; 4H006/AA01; 4H006/AB20; 4H006/UA13; 4H006/UA42; 4H006/UA51; 4H006/UA52
US 2004072804	NCL	514/167.000
	ECLA	A61K031/56; A61K031/59

OS MARPAT 135:304063

GI



AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = alkyl, hydroxyalkyl, fluoroalkyl; R4 = H, Me, acyl, OH, any of the typical side chains known for vitamin D type compds., etc.] are prepared

These compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and had a VDR binding ratio of 5.5, and HL-60 differentiation ED50 of 1.1 x 10-10 M.

ST vitamin D homologated epi alkyl nor prepn osteoporosis; antitumor vitamin D homologated epi alkyl nor prepn

IT Biological transport
(calcium; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Prostate gland
(carcinoma, inhibitors; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Intestine, neoplasm
(colon, inhibitors; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(colon; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(leukemia; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(mammary gland; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Mammary gland
(neoplasm, inhibitors; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Bone, disease
(osteodystrophy; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
Osteomalacia
Psoriasis
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 9,10-Secosteroids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Vitamin D receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Antitumor agents
(prostate carcinoma; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT Osteoporosis
(therapeutic agents; preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 213319-30-3P 213332-83-3P 217446-51-0P 217446-52-1P 217446-53-2P
217446-54-3P 217446-55-4P 217446-56-5P 364059-45-0P
364059-49-4P 364059-50-7P 364059-52-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

IT 135711-62-5 144848-24-8 213250-67-0 364059-41-6 364059-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

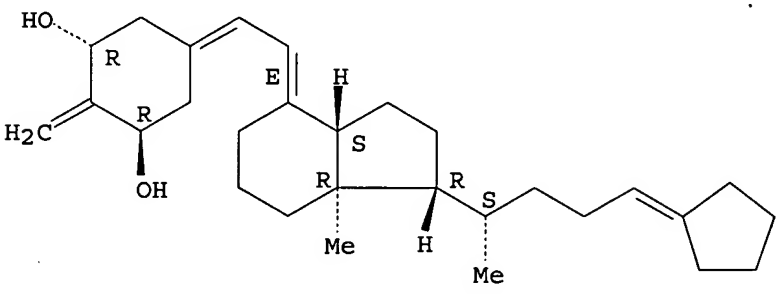
IT 213250-58-9P 213250-59-0P 213250-60-3P 213250-61-4P 213250-62-5P
213250-63-6P 213250-64-7P 213250-65-8P 213250-68-1P 213250-69-2P
213250-70-5P 213319-29-0P 364059-42-7P 364059-43-8P
364059-44-9P 364059-47-2P 364059-48-3P **364059-51-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Mikami, K; SYNLETT 1999, V12, P1899
(2) Sicinski, R; J MED CHEM 1998, V41(23), P4662 HCAPLUS
(3) Winconsin Alumni Research Foundation; WO 0010548 A 2000
(4) Wisconsin Alumni Research Foundation; WO 9000541 A 1990 HCAPLUS
(5) Wisconsin Alumni Research Foundation; WO 9841500 A 1998 HCAPLUS

IT **364059-49-4P 364059-50-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

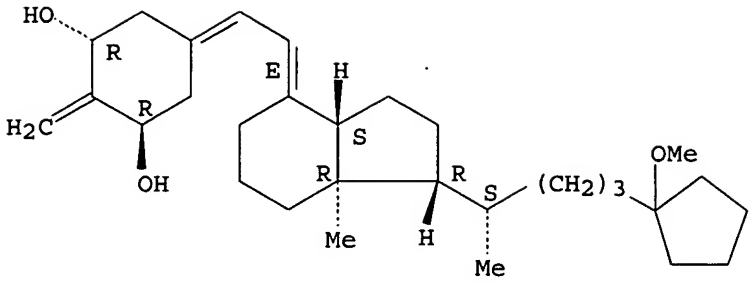
RN 364059-49-4 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-cyclopentylidene-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-50-7 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-methoxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

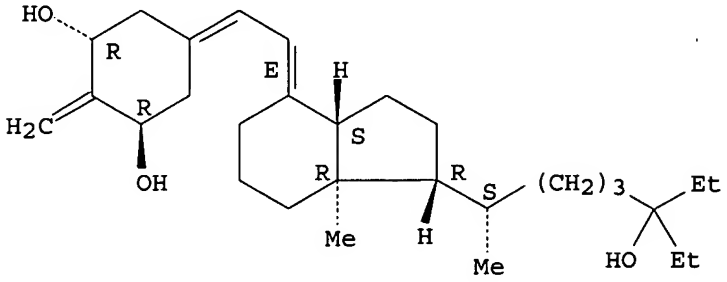
Absolute stereochemistry.
Double bond geometry as shown.



IT **364059-44-9P 364059-51-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

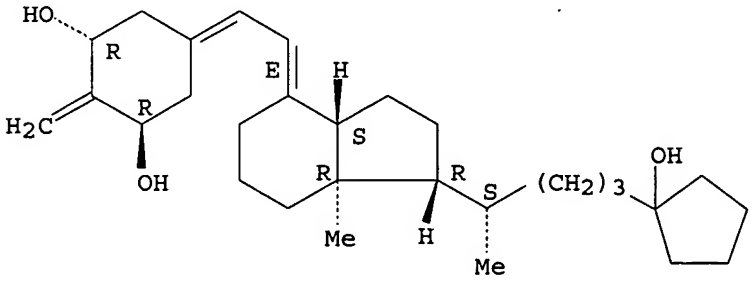
RN 364059-44-9 HCAPLUS
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1S)-5-ethyl-5-hydroxy-1-methylheptyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-methylene-, (1R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 364059-51-8 HCAPLUS
CN 19-Nor-9,10-secochola-5,7-diene-1,3-diol, 24-(1-hydroxycyclopentyl)-2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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               SEL RN

     FILE 'REGISTRY' ENTERED AT 15:14:13 ON 05 AUG 2005
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L3             8 S L2 AND C5-C6/ES AND 46.150.1/RID AND 3/NR
L4             5 S L2 AND C5-C6/ES AND 46.150.1/RID AND C5/ES AND 4/NR
L5             1 S L3 AND C29H48O3
L6            51 S C29H48O3 AND C5-C6/ES AND 46.150.1/RID
L7            49 S L6 AND 3/NR
L8             3 S L4 NOT SI/ELS
L9          1884 S C30H48O3 OR C29H46O3 OR C29H44O2
L10            4 S L9 AND C5-C6/ES AND 46.150.1/RID AND C5/ES AND 4/NR
L11            3 S L10 NOT 114694-10-9
L12            4 S L5,L8,L11
               SAV L12 QAZI780/A

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